1098-115 **N-T Pro-BNP Is a Powerful Predictor of Outcome in Patients With Stable Angina: A Substudy of the IONA Trial**

Stephen D. Robb, Theresa A. McDonagh, Michele Robertson, Ian Ford, Kim M. Fox, W. Stewart Hillis, John J. Morton, Henry J. Dargie, University of Glasgow, Glasgow, United Kingdom, Imperial College, London, United Kingdom

Background: Levels of B-type natriuretic peptide (BNP) have been shown to predict outcome in heart failure, asymptomatic left ventricular systolic dysfunction and acute coronary syndromes. The prognostic value of BNP and the related peptide N-terminal proBNP have never been reported in stable angina. We report the relationship between NT-proBNP and outcome in participants in the IONA study.
Methods: The IONA (Impact of Nicorandil in Angina) study was a randomised, placebo controlled trial of nicorandil in stable angina, involving 5126 patients. It showed that the addition of nicorandil 20mg twice daily to standard antianginal therapy reduced major adverse coronary events. Plasma levels of NT-proBNP were measured at randomisation in a subset of 1427 of the participants in this trial. The demographics in this peptide subgroup were similar to the whole study group. A Cox model was used, splitting the group into two halves above and below the median value for NT-proBNP, to relate NT-proBNP levels to the main end points of the study.
Results: Median levels of NT-proBNP were significantly higher in patients with each of the study endpoints: acute coronary syndrome – 531.5 v 188.0 pg/ml; coronary heart disease death or non fatal myocardial infarction (M.I.) - 728.0 v 190.5 pg/ml, and all cause mortality - 706.5 v 191.0 pg/ml (all P<0.0001). Baseline levels of NT-proBNP were shown to be predictive of each of the endpoints: acute coronary syndromes - HR 1.69 (1.31 – 2.18); coronary heart disease death or non fatal M.I. - HR 3.86 (2.29 – 6.29) and all cause mortality - HR 3.26 (2.00 – 5.33).
Conclusion: In patients with stable angina enrolled into the IONA trial circulating levels of NT-proBNP were a very powerful outcome indicator and could prove useful in assigning prognosis in patients with stable angina.

1098-116 **Serum Amyloid A Low-Density Lipoprotein Complex: A Novel Prognostic Marker in Stable Coronary Heart Disease**

Makoto Sahara, Ken Ogasawara, Tadanori Aizawa, Yoichirou Wada, Tatsuhiko Kodama, Shinichi Mashiba, Kazuo Uchida, The Cardiovascular Institute, Tokyo, Japan, Research Center for Advanced Science and Technology, The University of Tokyo, Tokyo, Japan

Purpose and methods: Although some reports have indicated that acute phase proteins such as C-reactive protein (CRP) and serum amyloid A (SAA) can predict the prognosis in patients with acute coronary syndrome, the value of these markers in stable coronary heart disease is still unclear. In this prospective cohort study, we evaluated SAA-LDL complex as a new marker for prediction of prognosis in addition to the ordinary markers including CRP, SAA and use of HMG-CoA reductase inhibitors or aspirin in consecutive 140 patients with stable coronary heart disease who had at least 1 coronary artery stenosis at the diagnostic coronary angiography (CAG). All the patients were followed up for 18 months after CAG. Serum levels of SAA-LDL complex were measured by sandwich enzyme-linked immunosorbant assay. **Results:** End-point events occurred in 21 patients (2 deaths from myocardial infarction, 2 cerebral infarctions and 17 coronary revascularization procedures). Age, diabetes mellitus, triglyceride and SAA-LDL complex were selected as independent predictors by a multiple stepwise regression test. The result of a logistic regression test was as follows.

	Odds ratio	Confidence interval
Age (year)	1.14	1.05-1.25
Diabetes mellitus	3.50	1.08-11.40
Triglyceride (10mg/dl)	1.12	1.01-1.23
SAA-LDL complex (10μg/ml)	2.32	1.05-4.70

Conclusions: Serum level of SAA-LDL complex can be a new marker for prediction of prognosis in patients with stable coronary heart disease. It is also suggested that SAA combined with LDL may play an important role in the process of atherosclerosis.

ORAL CONTRIBUTIONS

822 Acute Coronary Syndromes: Prognosis

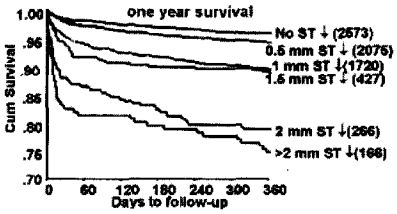
Monday, March 31, 2003, 2:00 p.m.-3:30 p.m.
McCormick Place, Room S106

2:00 p.m.

822-1 **Does the Extent of ST-Segment Depression Predict Short- and Long-Term Mortality in Patients With Non-ST Segment Elevation Acute Coronary Syndromes? Insights From the GUSTO IV**

Yuling Fu, Michael Lauer, Wei-Ching Chang, Robert M. Califf, Maarten L. Simoons, Lars Wallentin, Eric J. Topol, Paul W. Armstrong, for the GUSTO IV Investigators, University of Alberta, Edmonton, AB, Canada

ST depression (ST dep) >0.5 mm is widely used for risk stratification. However, the extent of ST dep as a predictor of short and long term mortality in NSTEMI acute coronary syndromes (ACS) is not well studied. Methods: 7741 of 7780 patients (pts) with ACS in GUSTO IV had baseline ECGs read in a core lab blinded to outcomes. ST dep was assessed in 0.5 mm increments. Results: 300 pts (3.9%) died at 30 days and 644 (8.3%) by 1 year. Pts with ECG confounders (514) had 30-day and 1-year mortality of 8.9% and 18.3%, respectively. There was an increased risk of death with each 0.5 mm increment in ST dep (Figure). After adjusting for baseline characteristics, troponin (TnT), and C reactive protein (CRP), the extent of ST dep was the most powerful predictor of 30-day death and the second most powerful at 1 year after age. ST quantitative analysis vs conventional cut point of >= 0.5 mm improved the ECG predictive power for 30-day and 1-year mortality to 20.8% and 10.2% vs 7.3% and 4.0%, respectively. The relative contribution of baseline biomarkers to mortality were: (a) 4.4% for TnT at 30days, which was 22.7% of the predictive power of ST dep; and (b) 3.6% and 2.1%, respectively, for TnT and CRP at 1 year, which were 36.7% and 21.7% of the predictive power of quantitative ST dep. Conclusion: Quantitative ST analysis provides major incremental prognostic insight over dichotomous assessment of >=0.5mm. Despite enthusiasm for new biomarkers, it is superior to TnT at 30 days and a more significant mortality predictor than either TnT or CRP at 1-year.



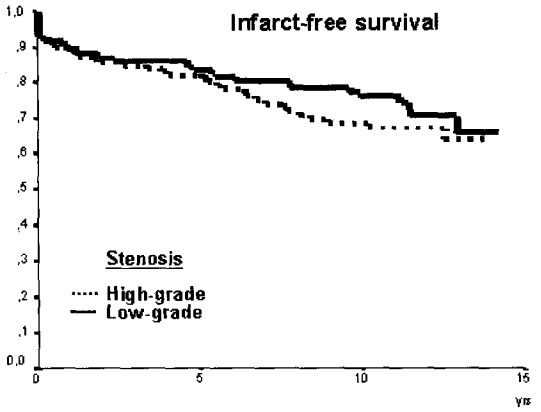
2:15 p.m.

822-2 **A High-Grade Stenosis After Successful Fibrinolysis Does Not Predict Death and Reinfarction: 10-Year Follow-Up of the APRICOT-1 Trial**

Marc A. Brouwer, Peter C. Kievit, Gerrit Veen, Freek W. A. Verheugt, Free University Medical Center, Amsterdam, The Netherlands, Heartcenter, University Medical Center, Nijmegen, The Netherlands

Background: In lack of randomized trials in the current era, the potential benefit of a routine invasive strategy on outcome following successful fibrinolytic therapy is uncertain. This study addresses the impact of a high-grade stenosis on both short-and long-term clinical outcome in the setting of a conservative revascularization strategy.
Methods: In the APRICOT-1 trial (1987-1991) 248 patients had fibrinolysis for suspected acute myocardial infarction with a patent infarct artery at 24-hour angiography, and follow-up angiography at 3 months. QCA-analysis was possible in 240 patients, a > 60% considered significant. Revascularization rate at 3 months was 11%.
Results: Death and/or reinfarction rates at 3 months were 8% for those with a significant stenosis and 10% for those with a < 60% stenosis at baseline (p=ns). Long-term infarct-free survival did not differ either (figure).
Conclusion: These observations challenge the hypothesis that patients with a high-

grade stenosis 24 hours after successful fibrinolysis are at increased risk for death and reinfarction, and -with it- the potential benefit of a routine invasive strategy.



2:30 p.m.

822-3 **Six-Month Mortality Rates Are Lower in Patients With an Acute Coronary Syndrome Treated With the Combination of Clopidogrel and a Statin Than in Patients Treated With Either Therapy Alone: An Analysis From the Global Registry of Acute Coronary Events**

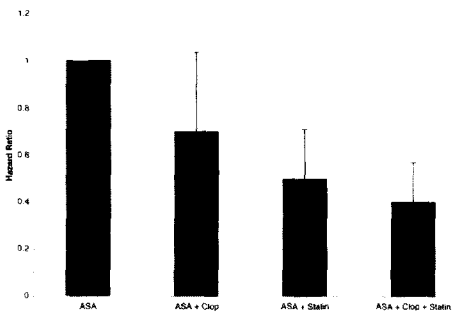
Michael J. Lim, Frederick A. Spencer, Joel M. Gore, Omar H. Dabbous, Eva M. Kline-Rogers, Robert J. Goldberg, Donna DiBenedetto, Kim A. Eagle, Rajendra H. Mehta, on behalf of the GRACE Investigators, University of Michigan Health System, Ann Arbor, MI, University of Massachusetts Medical School, Worcester, MA

Background: The use of clopidogrel as well as statins has been shown to prevent recurrent adverse events in patients with acute coronary syndromes. However, recent in-vitro data suggest that the antiplatelet effects of clopidogrel may be mitigated by the concomitant use of a statin. We hypothesized that, if these drug interactions are clinically relevant, then the mortality reduction in patients receiving both of these agents would not be as great.

Methods: Utilizing the GRACE database, 6-month mortality and stroke were evaluated in 4 groups based on discharge treatments: Group I=aspirin (ASA) alone (n=2956), Group II=ASA+clopidogrel (n=670), Group III=ASA+statin (n=2557), and Group IV= ASA+statin+clopidogrel (n=1229).

Results: Overall mortality for the patients treated with aspirin was 7.2%, compared to 4.8% in Group II, 4.2% in Group III, and 3.0% in Group IV. There was a trend toward reduced stroke rate with combination therapy(1.3%, 1.7%, 1.2% and 0.7%, respectively). Utilizing a Cox regression model, hazard ratios and 95% confidence limits were computed for mortality at 6 months compared to treatment with aspirin alone (Fig).

Conclusions: These data suggest that, if there is a pharmacologic interaction between statin medications and clopidogrel, it is not apparent in 6-month mortality rates within the GRACE registry patients. In fact, there is a trend toward reduced mortality in those patients receiving aspirin+clopidogrel+statin compared to the other groups, suggesting a synergistic effect.



2:45 p.m.

822-4 **Which Features of the Metabolic Syndrome Predict Clinical Outcomes (Death/Myocardial Infarction) in Patients With Angiographic Coronary Artery Disease?**

Heath U. Jones, Joseph B. Muhlestein, John F. Carlquist, Benjamin D. Horne, Robert R. Pearson, Chloe A. Allen Maycock, Sandra P. Reyna, Tami L. Bair, Donald L. Lappé, Dale G. Renlund, Jeffrey L. Anderson, LDS Hospital, Salt Lake City, UT, University of Utah, Salt Lake City, UT

Background: The metabolic syndrome (MS), a clustering of dyslipidemia, dysglycemia, hypertension, and obesity, is regarded as an important risk factor for coronary artery disease (CAD) onset. The Adult Treatment Panel III recently provided a uniform definition of MS, but the predictive value (PV) of MS and its components for cardiovascular events once CAD has developed is unknown.

Methods: We prospectively tested the PV of MS and its components for incident death or myocardial infarction (D/MI) in patients (pts) with advanced CAD (≥70% stenosis). Acute MI at presentation was excluded. Components of the MS assessed at baseline included: 1) fasting glucose (FG) ≥110 mg/dL, 2) triglycerides (TG) ≥150 mg/dL, 3) high density lipoprotein (HDL) <40 mg/dL in men or <50 mg/dL in women), and 4) systolic blood pressure (SBP) ≥130 and/or diastolic BP ≥85 mmHg. MS was defined as ≥3 features. Waist measurement was not available, but body mass index (BMI ≥27 kg/m2) was explored as a surrogate measure. Analysis used multivariable Cox regression.

Results: The study cohort was 2,037 pts; 76% were male; average age was 65±11 y; 17% had a prior MI and 8% had heart failure (HF). MS was present in 51% (high FG: 45%, high TG: 53%, low HDL: 74%, high S/DBP: 77%). High BMI was present in 57%. In contrast to our prior finding that MS predicts CAD diagnosis, MS failed to predict D/MI in pts with existing CAD (p=0.81). Only high FG , a MS component, predicted D/MI (hazard ratio [HR] 1.41, 95% CI 1.14-1.74, p=0.002). (Clinical diagnosis of diabetes was even better than FG: HR 1.92, p<0.001). High TG, low HDL, and high S/DBP were not predictors (p=0.2-0.3). Likewise, high BMI did not predict risk. In multivariable modeling, D/MI was predicted by age (p<0.001), high FG (HR=1.38, CI 1.12-1.71, p=0.003), and high S/DBP (HR=0.72, CI 0.57-0.91, p=0.006). (The PV of S/DBP disappeared when pts with HF and prior MI were excluded).

Conclusion: Once CAD is established, high FG alone, but not MS, distinguishes subsequent prognosis (D/MI). This extends previous observations of reduced PV for several established risk factors (e.g., gender, hyperlipidemia, smoking, hypertension, but not diabetes) when applied to secondary as compared to primary risk assessment.

3:00 p.m.

822-5 **Clinical and Angiographic Predictors of Cardiac Events in Patients With Non-ST Elevation Acute Coronary Syndromes Undergoing Percutaneous Coronary Intervention in the Current Era: Insights From the PRESTO Trial**

Heidar Arjomand, James T. Willerson, David R. Holmes, Bassam Roukoz, Satish Surabhi, Ismail Dairywala, Chowdhury Ahsan, Marc Cohen, Zoltan G. Turi, Sheldon Goldberg, Drexel University College of Medicine, Philadelphia, PA, Mayo Clinic, Rochester, MN

Background: Patients with non-ST elevation acute coronary syndromes (NSTE-ACS) represent a high-risk group of patients. An early invasive strategy with percutaneous coronary intervention (PCI) is recommended in these patients. However, there is limited data on predictors of outcome in ACS patients undergoing PCI in the current era.

Methods: We identified clinical and angiographic predictors of outcome in 5,503 consecutive patients with NSTE-ACS who underwent PCI between April 1999 and July 2000 as a part of the Prevention of Restenosis with Tranilast and its Outcomes (PRESTO) trial.

Results: At 9-month follow-up, 18.4% of patients experienced a cardiac event (death, MI, or TVR). Multivariate analysis identified several clinical and angiographic predictors of a cardiac event (Table).

Conclusions: In patients with ACS undergoing PCI, certain clinical characteristics and angiographic features predict a high risk of adverse outcome.

Table 1. Clinical and Angiographic Predictors of Cardiac Events at 9 months.

	Odds ratio (95% CI)	p-value
Clinical Variables:		
- Diabetes	1.34 (1.15-1.56)	< 0.01
- Prior CABG	1.35 (1.12-1.62)	< 0.01
- Prior PCI	1.39 (1.15-1.68)	< 0.01
Angiographic Variables:		
- Bifurcation lesion	1.33 (1.06-1.67)	0.01
- Multivessel CAD	1.51 (1.06-2.15)	0.02
- Restenotic lesion	1.58 (1.27-1.98)	< 0.01
- Ostial lesion	1.74 (1.38-2.19)	< 0.01